

**Amendments to the Specification:**

Please amend the title as follows:

~~--AGENT CONTAINING NFκB DECOY FOR PROTECTING GRAFT AGAINST~~  
~~NEOINTIMAL THICKENING~~ AGENTS FOR PROTECTION FROM NEOINTIMAL  
FORMATION IN GRAFTS COMPRISING AN NFκB DECOY--

Please amend the paragraph on page 2, line 28 through page 3, line 13, beginning, "Gene expression is controlled by transcription factors that bind to the transcriptional..." as follows:

--Gene expression is controlled by transcription factors that bind to the transcriptional regulatory regions of genes. NFκB protein, which is known as a transcription factor, is a heterodimer protein comprising p65 and p50 subunits (Sen R. *et al.*, Cell 46: 705-16 (1986). NFκB is thought to function as a primary response switch when cells are externally stimulated. When NFκB is expressed in cytoplasm, it is activated by phosphorylation, migrates to the nucleus, and binds to a specific nucleotide sequence on the genomic DNA, called a "κB motif", which comprises about ten nucleotides. It then activates the transcription of various genes. Genes known to be transcribed upon NFκB stimulation include: (1) cytokines such as interleukin-1, -2, -3, -6, -8, and -12, tumor necrosis factor-α (TNF-α), lymphotoxin-α and interferon-α, (2) receptors for granulocyte colony-stimulating factor, monocyte-macrophage colony-stimulating factor, granulocyte-monocyte/macrophage colony-stimulating factor, interleukin-2, and such, (3) stress proteins such as complement factor B, -C3, and -C4, and α1 acid glycoprotein, (4) leukocyte adhesion molecules such as intercellular adhesion molecule (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1) ~~ICAM-1, VCAM-1~~, E-selectin, (5) immunoregulatory molecules such as major

histocompatibility complex class I and II molecules, T cell receptor  $\alpha$  and  $\beta$ , and  $\beta 2$  microglobulin (Immunology Today 19: 80 (1998)).--

Please amend the paragraph on page 7, lines 11 through 19, beginning, "The NF $\kappa$ B decoys used in the present invention can be produced by chemical or biochemical..." as follows:

--The NF $\kappa$ B decoys used in the present invention can be produced by chemical or biochemical synthesis methods used in the usual production of oligonucleotide compounds. For example, NF $\kappa$ B decoys comprising nucleic acids can be produced by genetic engineering techniques, such as methods using a DNA synthesizer. Moreover, these nucleic acids can be amplified by PCR methods using synthesized DNA as a template as necessary, and also by inserting DNAs into appropriate cloning vectors. Furthermore, desired nucleic acids can be produced by digesting obtained nucleic acids with restriction enzymes and such, or by connecting them using DNA ligase and such. To stabilize these oligonucleotides in cells, the bases, sugars, and phosphate moieties of the nucleic acids can be chemically modified (alkylation, acylation, and such).--

Please amend the paragraph on page 10, lines 6 through 27, beginning, "Mongrel dogs (NRB; Nihon Nosan, Kanagawa, Japan or HBD; Oriental Yeast Corporation..." as follows:

--Mongrel dogs (NRB; Nihon Nosan, Kanagawa, Japan or HBD; Oriental Yeast Corporation, Osaka, Japan) weighing 18 to 20 kg and fed with a standard food were used. After anesthetizing the dogs with ketamine (5 mg/kg body weight, intramuscular injection), intratracheal intubation was performed. Saphenous vein grafts were collected from the left hind leg of the dogs, kept under general anesthesia by inhalation of 1.5% sevoflurane. To expose approximately 10 cm of the saphenous vein, the outer part of the legs was incised along the anteroposterior axis. The vein was cut from surrounding tissue using a "no touch technique" (Gottlob R., Minerca Chir. 32: 693-700 (1977)) and all side

branches were ligated with 4-0 silk ligature. The vein was then recovered from the dog and washed with heparinized 0.9% saline solution without distension (Angelini G. D. *et al.*, Cardiovasc. Res. 21: 902-7 (1987)). The above veins were then stored in the same solution at room temperature for about 60 minutes. A left fourth intercostal thoracotomy was performed, and a scrambled decoy (SD groups; n=5) or NF $\kappa$ B decoy (ND groups; n=5) solution (40  $\mu$ mol/L) was introduced into the vein graft wall by the method of Mann *et al.* (the pressure-mediated transfection; Proc. Natl. Acad. Sci. USA 96: 6411-6 (1999)) at ~~2000~~ 200 mmHg for 20 minutes (Fig. 1). After intravenous injection of heparin (100 U/kg body weight), the saphenous vein graft was interposed between the descending aorta (descending Ao.) and the left anterior descending coronary artery (LAD) without cardiopulmonary bypass and cardiac arrest (i.e., beating heart surgery). That is, an end-to-side anastomosis between the vein graft and the left anterior descending coronary artery was performed on the beating heart with 7-0 Prolene suture (Ethicon, Inc., USA) using an "Octopus" (Medotronic Inc., USA) stabilizer, and the other end of the vein graft was sutured to the descending aorta with 6-0 Prolene, in an end-to-side fashion. The LAD proximal region was sewn with 4-0 Prolene (Fig. 2).--

Please amend the paragraph on page 12, lines 13 through 22, beginning, "Proliferation of medial smooth muscle cells was immunohistochemically evaluated using..." as follows:

--Proliferation of medial smooth muscle cells was immunohistochemically evaluated using monoclonal antibodies against smooth muscle-specific  $\alpha$ -actin. Frozen sections (about 5  $\mu$ m thick) were prepared from a fresh-frozen tissue block, and monoclonal antibody against  $\alpha$ -actin specific to  ~~$\alpha$ -actin~~ smooth muscle (Histofine, Nichirei, Japan) was used. Immunohistochemical staining was performed using the immunoperoxidase, avidin-biotin complex system with nickel chloride color, and by a modified method of Bai *et al.* (Arterioscler.

Thromb. 14: 1846-53 (1994)). The staining result was measured using computerized image analysis software "NIH image". The  $\alpha$ -actin staining revealed a trend to inhibition of medial smooth muscle cell proliferation by transfection of the NF $\kappa$ B decoys (Figs. 3-3-a and 3-3-b).--

Please cancel the present "SEQUENCE LISTING", pages 1/3-3/3, and insert therefor the accompanying paper copy of the Substitute Sequence Listing, page 1, at the end of the application.